Acne Vulgaris

Multifactorial disorder of pilosebaceous unit.

***Pathogenesis*:**

1- Increase sebum production (seborrhea) due to hyper- response of the gland to androgenic stimulation.

2- Ductal hypercornification (comedone):

Excessive accumulation of ductal corneocytes due to →↑ production (formation) due to androgen stimulation OR due to ↓ separation (desquamation)

3- Proliferation of P. acne (anaerobic – facultative):

- Due to obstructed follicle + ↓O_2→good anaerobic medium→ colonization of P. acne.

- P. acne secrete lipase enzyme which cleave sebum into pro-inflammatory FFA, which are comedogenic and chemotactic.

4- Inflammation:

P. acne bind / activate toll- like receptors 2- 4 of the perifollicular inflammatory cells → induction of monocytes, keratinocytes, inflammatory cells → which secretes → proinflammation cytokines (TNFα, IL 1, 6, 8) → perifollicular inflammation.

N.B.: TLR are protein found in the transmembrane. They are for recognition of

P. acne components (peptidoglycan). They represented by monocyte + macrophages.

Role of estrogen in acne pathogenesis:

1- Antagonize the effect of androgens on s. gland.

2- Decrease in production of androgens by –ve feedback mechanism through inhibition of pituitary (GnRH).

3- Regulating genes that inhance S. gland growth or lipid production.

Role of other factors:

1- Genetic: +ve family history →↑ acne.

2- Diet: No proved studies but

- high glycemic food →↑ acne

- ↑ Milk →↑ acne cause it contain hormones and androgens.

3- Premenstrual period →↑ acne.

4- Stress ↑ acne. 5- UVR may ↑ or ↓.

6- Occupation →↑ hydration →↑ acne.

7- Sweating →↑ deterioration of acne.

Types of pilosebaceous follicle

[1] Terminal: Long – coarse – (scalp – beard – axilla – pubis), No acne develop cause powerful erection of erector pilli muscle can allow free sebum excretion.

[2] Sebaceous: Rudimentary hair follicle + large seb. gland, can't withstand sebum production →acne in (face – shoulders – upper back – sternal area).

[3] Vellous: fine – soft hair follicle core the all body at puberty it become terminal or sebaceous according to the site.

***Type of acne*:** C/P polymorphic

Comedone – popular – pustular – nodular – nodulocystic

Polymorphic but one type is peridominate.

Types of comedones:

Black head: (open comedone): Due to presence of melanin or oxidized sebum.

White head: (closed comedone) collection of sebum closed by plug of keratinization.

Intermediate: features of both black and white heads.

Sand paper: multiple small white head on for head.

Macro-comedone: > 1mm.

Submarine: > 0.5 cm.

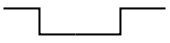
2ry: chloracne, steroid acne.

NB.: black head acne rare to be inflamed but white do.

Acne scars:

1- Hypertrophic (tissue formation) : keloids.

2- Hypotrophic tissue damage:

- Ice pick  - rolling  - box car. 

Grading of acne:

	Comedones	Papules / pustules	Nodules
Mild	≤ 25	≤ 10	-
Moderate	> 25	> 10 to ≤ 30	≤ 10
Sever	> 100	> 30	> 10

Acne Variants

(1) Post-adolescent acne: > 25 years. Lesion is

- Inflammed – tender – deep seated – papulonodules.
- Premenstrual flaring good response to hormone R/.
- Associated with smoking.

(2) Acne conglobata:

- 1ry defect: - Altered keratinization of seb. Follicle.
  - Leakage of retained smeat into tissue surrounding pillegecrine gland.
- Characterized by nodules: cysts (tender) that fuse together to form sinus + grouped multiple fused black heads (double, triple) + keloid scars, isotretinoin immediately – no need for sys. Steroid syst. Antibiotics is good.

(3) Acne fulminans (Acute febrile ulcerating acne conglobes with polyarthralgia) or (Leukemoid reaction) or (Acne Maligna).

- **Rare:** male 13 – 16 years – sudden.
- Looks like acne conglobate + high inflammatory lesion in upper chest, back.
- Hemorrhagic nodules + plaques which undergo suppurative degeneration → ulceration.
- Systemic symptoms is +ve

+ FHMA + myalgia, anaemia + lencocytosis ↑ ESR + Hepatomegaly.

- Bed rest – hospitalization.

– topical CST.

- Systemic R, isotretinoin alone or combined with CST, NSAIDs.

	Acne fulminans	Acne conglobate
Age	13-16 years	20- 25
Onset	Sudden	Slow
C/P	Hgic ulceration	Nodules, cysts, polyporous comedones
Systemic symptoms/ signs	Common F, M, ↑ESR, lencocytosis, proleinuria hepatomegaly, spleenomy, erythema nodusm, bone acne.	Un common
Response to systemic ABCs	No	Yes

(4) Gram negative folliculitis:

- Caused by prolonged R/ of AV with broad spectrum antibiotics.
- Superficial pustules grouped ground the nares or nodular cystic lesions.
- Culture shows: E. coli, klebsiella, pseudomonas.

- Stop antibiotic
- Give G-ve antibiotic.
- Isotretinoin in sever cases. Trimethoprim 1 x 2.

(5) Drug induced acne:

Drugs that ↑ AV or induce acne form eruptions:

e.g.: - Gonadotropins, Androgens, CST, Halthane.

- Phenobarbitone, phenytoin, Isoniazide, Rifampcim.
- Psoralen, sulphur, thiouracil.

Steroid acne: steroid →↑ keratininzation in upper part of seb. Duct C/P sudden appearance of inflamed papules, pustules and abscent comedones, rare in face the lesions are monomorphic than AV. Post inflammatory hyperpigmentation are common.

Stop steroid + tretinoin 0.05%.

(6) Neonatal Acne: in 20% of newborn. May be at birth or first few months. It's mild and regressive sites: nose, cheeks, forehead. Mainly comedonal/ no scaring pathogenesis / bt clear but may be associated with malassezia due to improvement when treated by ketocanazol 2% cream/ Maternal hromones may play a role.

(7) Infantile Acne: (3- 6 month) till 5 years, more in face mainly inflammatory may be sever, nodules, cysts – leave scaring pathogenesis: hormonal imbalance (↑LH, testo- DHEA) Minor role of maternal hormones.

(8) Acne mechanica: H physical trauma e.g. head band in sport men.

(9) Acne due to external chemical origin:

External chemical induce follicular hyperkeratosis

- Cosmetics: make up contain lanolin, petrolatum.
- Oils, tars.
- Chlor acne.
- Acne detergicans due to excessive wash by soap & stop wash + topical tretinoin.

(10) Acne excorice des jeunes filles:

AV with excoriachor in young females due to compulsive picking, squeezing of lesions (Neurotic) commonly associated with obsessive compulsive disorder (OCD) R/ doxepin or SSRIs.

(11) Solid facial edema (Morbihan's disease):

It's a complication of AV

C/ P distortion of midline face, cheeks, due to soft tissue swelling. The woody non scaling induration may be accompanied with erythema. No spontaneous resolution.

R/ Isotretinoin alone or with ketotilen.

(12) Endocrinologic abnormalities: check CH, FSH, DHAS, free, total KCTO.

(13) A pert syndrome:

A dominant mutation of $FGFR_2$.

- Acne form eruptions papules in entire extensor aspects of arm, thigh, buttocks, resistance to all therapeutics, but response to isotretinoin.
- Marked seborrhea, nail dystrophy, cutaneous, ocular, hypopigmentation.

(14) Vasculitic / Pyoderma gangrenosum acne:

- Wild acne → develop sever vasculitic, pyoderma gangrenosum – like lesion → heal with scar.
- No response to isotretinonin but response to oral steroid and azathioprine 200 (1 x 1 x 3 for 4 month).

Histopathology

Comedo: (Keratinous debris/ fragments of hair/ sebum + microorganism).

Closed (white) melanocyte is in laver portion with few melanin.

Open (black) large, active melanocyte with high melanin (oxidation of melanin).

Papules: lymphocytic perifollicular infiltration → rupture of follicular wall → escape of content into dermis:

- If small aggregation → Pustules.
- If large aggregation + deep → Nodule.

Treatment of acne

According to the type and severity

Mild (Mainly topical)		
Non inflammatory	**Inflammatory**	**Mixed**
Retinoid 0.05%	Benzyl peroxide	Benzyl peroxide
Azelaic	Azelaic	Erythromycin
Adapalene	Adapalene	Retinoid ABCs
Comedone extractor	Abcs (clindamycin erythromycin + zinc acetate)	azelaic

Moderate: topical + systemic (Abcs of cyproterone acetate).

Sever: Isotretinoin.

Topical treatment of acne

(1) Benzoyl peroxide: - Bacteriostatic (due to libration of free O)

- Comedolytic. - Feeling effect

S.E.: irritation + bleaching of clothes.

(2) Tretinoids:

- Comedolytic (resolve mature lesion + prevent new lesions).
- Enhance penetration of other drugs.

S.E.: irritation + photo – irritation.

M.O. action: cell cytoplasm it affects the gene expression.

- **Adapalene** is a static naphthoic acid with a potent pharmacology in controlling cell proliferation, differentiation less irritant than tretinoids.
- **Tazarotine:** Synthetic acetylenic retinoid once applied it converts to active form.

(3) Topical antibiotics (clindamycin / erythromycin)

But it may help in development of resistant strains of P. acne so we give erythromycin 4% + zinc acetate (Acne biotic or Zineryl) which inhibit this development.

(4) Azelaic acid: anti- acne through:

- Normalization of disturbed follicular keratinization.

- Antimicrobial action. - Anti- inflammatory action.

N.B.: No effect on seb. gland. Can be used as a peeling in melasma.

Advantages: - Less irritant than benzoyl peroxide or tretinoin.

- Doesn't produce resistant P. acne strains.

(5) Topical steroid: short time only in inflammatory acne.

(6) Topical dapsone: Dapsone gel.

Effective, safe, well tolerated, rapid onset of action, has anti- inflammatory action.

Systemic treatment of Acne

♦ **Antibiotics** ♦ **Hormones** ♦ **tretinoin** ♦ **antiandrogens**

(1) Antibiotics:

- ***Tetracycline*s:**

  - **Tetracyclin** (1g/ daily on empty stomach)

    contra- indicated in pregnancy, renal, hepatic.

  - **Doxycyclin** (100- mg/ day) S.E. (photosensitivity).

  - **Minocyclin:** S.E. (vertigo like syndrome).

S.E.: Black blue pigmentation, metalic taste, hypersensitivity syndrome reaction, induce SLE, iron limit efficacy.

- ***Macrolids*:**

  - Erythromycin Lg daily safe in pregnancy.

  - Azithromycin 3 tab weekly dt long half-life S.E. GIT upset.

- ***Trimethoprim sulfamethoxazole***: 400- 600 daily.- S.E. bone marrow suppression.

***Clindamycin*:** 150 mg 1 x 3 S.E.: Colitis.

Mechanism of action of antibiotics:

Inhibition of P. acne:

- ↓ lipase, ↓ chemotactic substance.

- ↓ complement pathway → ↓ Neutrophil migration.

(2) Hormones:

- Estrogen suppress ovarian androgens.
- Corticosteroids suppress adrenal androgens used as anti-inflammatory in sever, cystic acne, acne conglobate).
- Systemic anti-androgens.

(3) Anti-androgens:

(A) Cyproterone acetate:

synthetic non estrogenic compound that interfere with winding of androgens to it's target organs (seb. Gland/ hair bulb/ germinal tissue of gonads)

Indication: females with seborrhea, AV, Androgenic Alopecia, Hirsutism.

SE: inhibition of ovulation / spermatogenesis/ weight gain hypospadias/ inhibition of scrotal development.

Contra-Ind: male/ pregnant female.

Dose: 1 x 1 → start from day 5 of menstruation to day 25 for 3-12 month.

Diane: Diane – 35 androcur 10, 50 .

(B) Spironolactone 50/ 200 mg/ day.

(C) Ketocorazole/ cimetidine.

(4) Oral retinoids:

- Indications: - Most types of acne. - G –ve folliculitis.
- Rosocea. - Fordyce's disease.
- Hidradenitis' suppuration - Pyoderma faciale.

- Mechanism of action:

- Sebum suppression. - P. acne reduction.
- Normalization of follicular epithelial desquamation.
- Anti-inflammatory: through
  - Block the release of proinflammatory cytokines.
  - Inhibit leucocytic migration.
  - Block cellular inflammation.

- Dose 0.5- 1 mg/kg for 4- 5 months.

N.B.: Cumulative dose 120- 150 mg/ kg.

- **S.E.:** teratogenicity – Acne flare- chelitis – conjunctivitis, Nasal dryness- dermatitis, elevated liver function test – depression inflammatory bowel disease – headache – arthralgia – myalgia.

When to stop tretinoids;

- ↑ liver enzyme more than 3 times.
- ↑ T.G. more than 800.
- Pt develop IBD (rectal bleeding – pain – diarrhea).

Other lines of treatment of acne:

(1) Physical:

- Acne R with light.

Blue light → anti- inflammatory.

Photodynamic therapy (PDT).

- Extraction of comedones:

By extractor, light cautry, cryotherapy,

IL steroid for nodulocystic lesion.

(2) Treatment of Acne scars:

- Ice pick (punch excision – elevation, grafting laser derma brasion – spot TCA peel).
- Rolling (micrograft + subcision / filler / laser derma brasion – deep spot TCA cross peel).
- Boxcar (laser / punch excision / fractional CO_2 laser).
- Keloid (IL corticosteroids, then Imiquimod after IL/ cryotherapy / electrotherapy.
- Hypertrophic (IL CST the same as a keloid).

(3) Derma roller/ micro needling / collagen inducation therapy.

(4) Platelet rich plasma (PRP).

(5) CO_2 Laser.